

## BEST AVAILABLE COPY

following:

a<sup>1</sup> ~~--~~In certain embodiments, the T helper peptide is one that is recognized by T helper cells present in the majority of the population. This can be accomplished by selecting amino acid sequences that bind to many, most, or all of the HLA class II molecules. These are known as "loosely HLA-restricted" or "promiscuous" T helper sequences. Examples of peptides that are promiscuous include sequences from antigens such as tetanus toxoid at positions 830-843 (QYIKANSKFIGITE; SEQ ID NO:2382), *Plasmodium falciparum* circumsporozoite (CS) protein at positions 378-398 (DIEKKIAKMEKASSVFNVVNS; SEQ ID NO:2383), and *Streptococcus* 18kD protein at positions 116 (GAVDSILGGVATY<sup>1</sup>GAA; SEQ ID NO:2384). Other examples include peptides bearing a DR 1-4-7 supermotif, or either of the DR3 motifs. ~~--~~

Please replace the paragraph beginning at page 51, line 12, with the following:

a<sup>2</sup> ~~--~~Alternatively, it is possible to prepare synthetic peptides capable of stimulating T helper lymphocytes, in a loosely HLA-restricted fashion, using amino acid sequences not found in nature (*see, e.g.*, PCT publication WO 95/07707). These synthetic compounds called Pan-DR-binding epitopes (*e.g.*, PADRE<sup>TM</sup>, Epimmune, Inc., San Diego, CA) are designed to most preferably bind most HLA-DR (human HLA class II) molecules. For instance, a pan-DR-binding epitope peptide having the formula: aKXVAAWTLKAAa (SEQ ID NO:2385), where "X" is either cyclohexylalanine, phenylalanine, or tyrosine, and "a" is either D-alanine or L-alanine, has been found to bind to most HLA-DR alleles, and to stimulate the response of T helper lymphocytes from most individuals, regardless of their HLA type. An alternative of a pan-DR binding epitope comprises all "L" natural amino acids and can be provided in the form of nucleic acids that encode the epitope. ~~--~~

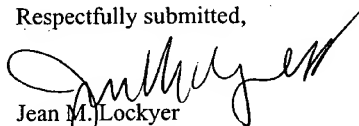
Please replace the pages set forth below with the substitute pages attached hereto in Appendix B. Marked up copies of the pages showing amendments are provided in Appendix A.

Please substitute page 100 (Table IV), the attached Substitute Sheet, page 100.

Please substitute page 101 (Table V) with the attached Substitute Sheet, page 101.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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